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August 24, 2004

Gavin T. Bogle Senior Patent Attorney Wyeth 87 Cambridge Drive Cambridge, MA 02140

Re:

U.S. Patent Application Serial No. 10/051,841

Inventors: Kathleen H. Young et al.

Filed: January 17, 2002

Title: Methods For Identifying Modulators of N-Type

Ion Channel Inactivation

Your Ref.: AHP98133 C1; Our Ref.: 31896-69100

Dear Gavin:

Enclosed is a copy of an Office Action dated August 11, 2004 which has been received from the U.S. Patent and Trademark Office in connection with the above-identified application.

A response is due in the U.S. Patent Office no later than November 11, 2004. Extensions of time up to February 11, 2005 can be obtained in monthly increments upon payment of appropriate extension fees to the U.S. Patent Office.

We have reviewed the application to confirm consideration by the Examiner of the Information Disclosure Statement filed January 17, 2002. The Examiner has considered all references submitted.

In the Action, pending claims 39-44 (previously a Group VII election) were rejected for various reasons. For example, claims 39-40, and 43-44 were rejected under 35 U.S.C. §101, but were indicated as acceptable subject matter if additional limitations were added. Claims 39-44 were rejected under 35 U.S.C. §112, first paragraph, for nonenablement and failure to adhere to the written description requirement. Claims 39, 41 and 43 stand rejected under 35 U.S.C. §102(b) as being anticipated by the sequence set forth in Accession No. M26161 (Sequence Comparison A) by Christie et al. (from a Science article). Similarly, claims 39-44 were rejected

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Gavin T. Bogle August 24, 2004 Page 2

under §102(b) as being anticipated by the sequence set forth in Accession No. M60450 (Sequence Comparisons B and C) Tamkun et al. (from a *FASEB* article). Lastly, claims 40, 42 and 44 were rejected under §102(b) as being anticipated by the sequence set forth in Accession No. X83127 (Sequence Comparison D) by Leicher et al. (from a *Neuropharmacology* article).

We would also like to remind you of the fact that the period for submission of prior art of three months from the later of its date of first citation by another patent office or its having come to the attention of anyone involved in the preparation or prosecution of this application is not extendible, so that any additional art which has or should come to your attention should be promptly forwarded to us in time for it to be filed within that three-month period if a late fee is to be avoided.

Further, as with all applications, it is necessary to bring to the attention of the Examiner all pending U.S. applications and/or patents which disclose subject matter relevant to the subject matter of the present application. Accordingly, please inform us of any such related pending U.S. applications and/or patents of which we might not be aware so that we may bring them to the Examiner's attention.

Best regards.

Very truly yours,

NIXON PEABODY LLF

Raymond Van Dyke

RVD/kw Enclosures

cc: Kay Brady (w/encl.)



United States Patent and Trademark Office

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,841	01/17/2002	Kathleen H. Young	AHP 98133 C)	2237
22204 7	590 08/11/2004	Companies and Companies	EXAMINER	
NIXON PEABODY, LLP 401 9TH STREET, NW SUITE 900 WASHINGTON, DC 20004-2128		AUG 1 3 2004	MURPHY, JOSEPH F	
			ART UNIT	PAPER NUMBER
			1646	
		t to	DATE MAIL ED. 09.0 1/2004	

Please find below and/or attached an Office communication concerning this application or proceeding.

	Application No.	Amplianettal			
	Application No.	Applicant(s)			
089 4-41 0	10/051,841	YOUNG ET AL.			
Office Action Summary	Examiner	Art Unit			
	Joseph F Murphy	1648			
- The MAILING DATE of this communication appears on the cover sheet with the correspondence address - Period for Reply					
A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. - Extensions of time may be evaliable under the provisions of 37 CFR 1.138(e). In no event, however, may a reply be timely filed after SIX (8) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Fellure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (36 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).					
Status					
1) Responsive to communication(s) filed on 19 May 2004.					
2a)☐ This action is FINAL. 2b)☑ This action is non-final.					
3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is					
closed in accordance with the practice under Ex parte Quayte, 1935 C.D. 11, 453 O.G. 213.					
Disposition of Claims					
4) Claim(s) <u>39-44</u> is/are pending in the application.					
4a) Of the above claim(s) is/are withdrawn from consideration.					
5) Claim(s) is/are allowed.					
6)⊠ Claim(s) <u>39-44</u> is/are rejected.					
7) Claim(s) is/are objected to.					
8) Claim(s) are subject to restriction and/or election requirement.					
Application Papers					
9) The specification is objected to by the Examiner.					
10)☐ The drawing(s) filed on is/are: a)☐ accepted or b)☐ objected to by the Examiner.					
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).					
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d),					
11) The oath or declaration is objected to by the Ex	aminer. Note the attached Of	fice Action or form PTO-152,			
Priority under 35 U.S.C. § 119	,				
12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).					
a) ☐ All b) ☐ Some * c) ☐ None of:					
1. Certified copies of the priority documents have been received.					
2. Certified copies of the priority documents have been received in Application No					
3. Copies of the certified copies of the priority documents have been received in this National Stage					
application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received.					
See the attached detailed Office action for a list	or the cardined copies hot rec	eived.			
Attachment(e)					
1) Notice of References Cited (PTO-892)	4) Interview Summ				
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)	Paper No(s)/M: 5) Notice of Inform	all Date Tot Patent Application (PTO-152)			
Been Ne/a/Mail Date 04172002	e) 🔽 Other Comme	n Communicano A D			

Art Unit: 1646

NO. 4940 P. 5 RECEIVED CENTRAL FAX CENTER AUG 2 Page 2 2 0 2004

DETAILED ACTION

OFFICIAL

Election/Restrictions

Applicant's election of Group VII, claims 39-44, in the Reply filed 5/19/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 39-40, 43-44 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 39-40 are directed to polynucleotides, but do not contain a limitation wherein the polynucleotide is isolated therefore the claims read on a product of nature. Claims 43-44 as written are directed to host cells comprising a polynucleotide. Since these claims do not contain a limitation wherein the host cells are isolated, the claims read on a transgenic human, which is not patentable subject matter. This rejection could be obviated by addition of a limitation wherein the host cell is isolated.

Art Unit: 1646

Page 3

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 39-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for a full-length polynucleotide sequence of SEQ ID NO: 3, 4, 7, 8; and a polynucleotide sequence 90% identical to SEQ ID NO: 3, 4, 7, 8 wherein the encoded polypeptide which binds to an amino-terminal inactivation region of hKv\(\beta\)1 protein, or the intracellular receptor region of an \(\alpha\)-subunit of a hKvl.1 protein, does not reasonably provide enablement for a polynucleotide sequence 90% identical to SEQ ID NO: 3, 4, 7, 8 wherein the encoded polypeptide which binds to an amino-terminal inactivation region of an ion channel protein, or the intracellular receptor region of an \(\alpha\)-subunit of a voltage-gated ion channel. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims,

The claims are drawn to polynucleotide sequences that are 90% identical to sequences as set forth in the specification. The claims are overly broad since insufficient guidance is provided as to which of the myriad of variant nucleic acids encode polypeptides which will retain the characteristics of SEQ ID NO: 3, 4, 7, 8. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible encoded muteins of the proteins which are encoded by SEQ ID NO: 3, 4, 7, 8. The claims are directed to variant polypucleotides encoding variant polypeptides. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, as an example of the unpredictable effects of mutations on

Art Unit: 1646

Page 4

protein function, Mickle et al. (Mickle JE et al. Genotype-phenotype relationships in cystic fibrosis. Med Clin North Am. 2000 May;84(3):597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (Voet et al. Biochemistry. 1990. John Wiley & Sons, Inc. pages 126-128 and 228-234) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Additionally, Yan et al. teaches that in certain cases, a change of only two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Twoamino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. Science 290: 523-527, 2000). Since the claims encompass variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would

Application/Control Number: 10/051,841

Art Unit: 1646

require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. While the claims set forth a functional limitation for the encoded variant polypeptides wherein the encoded polypeptide binds to an amino-terminal inactivation region of an ion channel protein, or the intracellular receptor region of an α-subunit of a voltage-gated ion channel, however, the Specification only teaches proteins which binds to an amino-terminal inactivation region of hKvB1 protein, or the intracellular receptor region of an \alpha-subunit of a hKv1.1 protein. Additionally, the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides and encoded polypeptides which the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polypeptides. Since the claims do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any meet the limitations of the claims. Thus, since Applicant has only taught how to test for

Application/Control Number: 10/051,841

Art Unit: 1646

polynucleotide variants encoding polypeptide variants, and has not taught how to make polynucleotides encoding polypeptide variants, it would require undue experimentation of one of skill in the art to make and use the claimed polynucleotides.

Claims 39-44 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in paper NO. 10, 9/26, 2002. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims are drawn to polynucleotide sequences that are 90% identical to sequences as set forth in the specification. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and

Application/Control Number: 10/051,841

Art Unit: 1646

because the genus is highly variant, a nucleic acid with a sequence as set forth in SEQ ID NO: 3, 4, 7, 8 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 39, 41, 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Christie et al. (1989).

Christie et al. teaches the cloning and expression of RBK-1. The predicted sequence of the 495-amino acid protein is homologous to potassium channel proteins encoded by the Shaker locus of Drosophila and differs by only three amino acids from the expected product of a mouse clone MBK-1. Messenger RNA transcribed from RBK-1 in vitro directed the expression of potassium channels when it was injected into Xenopus oocytes. The potassium current through the expressed channels resembles both the transient (or A) and the delayed rectifier currents reported in mammalian neurons and is sensitive to both 4-aminopyridine and tetraethylammonium. The sequence of the nucleic acid encoding the RBK-1 polypeptide, comprises SEQ ID NO: 3 (See Sequence Comparison A, attached), thus claim 39 is anticipated. Christie et al. further teaches vectors and host cells comprising this polynucleotide, thus claims 41, 43 are anticipated.

Application/Control Number: 10/051,841

Art Unit: 1646

Claims 39-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Tamkun et al. (1991).

Tamkun et al. teaches that full-length cDNA clones were isolated from human ventricular libraries that encode two voltage-gated K+ channels. These two cDNAs, designated HK1 and HK2, encode proteins of 653 and 605 amino acids, respectively. HK1 is the human equivalent (98% identity) of an inactivating K+ channel previously described in rat heart (RHK1) whereas the HK2 channel is 86% identical to a cloned rat brain K+ channel (Kv1). The sequence of the polynucleotide encoding the potassium channel comprises SEQ IUD NO: 4 and 8 (See Sequence Comparison B, C attached) thus claims 39-40 are anticipated. The Tamkun reference further teaches the cloning of these polynucleotides into vectors and expression in host cells, thus claims 41-44 are anticipated.

Claims 40, 42, 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Leicher et al. (1996).

Leicher et al. analysed the structure of the human KCNA1B (hKv beta 1) gene. KCNA1B is > 250 kb in size and encodes at least three Kv beta 1 splice variants. The Kv beta 1 open reading frame is divided into 14 exons. In contrast, genes coding for family members of KCNA (Kv 1 alpha) subunits are markedly smaller and have intronless open reading frames. The expression of Kv 1 alpha and Kv beta mRNA was compared in Northern blots of poly(A+) RNA isolated from various human brain tissues. The polynucleotide of Leicher et al. comprises SEQ ID NO: 7 (see Sequence Comparison D, attached), thus claim 40 is anticipated. The Leicher

Art Unit: 1646

reference further teaches vectors comprising the sequence, and transfection of host cells, thus claims 42, 44 are anticipated.

Page 9

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Application/Control Number: 10/051,841

Art Unit: 1646

Information regarding the status of an application may be obtained from the Patent
Application Information Retrieval (PAIR) system. Status information for published applications
may be obtained from either Private PAIR or Public PAIR. Status information for unpublished
applications is available through Private PAIR only. For more information about the PAIR
system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private
PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOSEPH MURPHY

Joseph F. Murphy, Ph. D. Patent Examiner Art Unit 1646 July 27, 2004

Sequence Comparison A

```
PREULT 5
RATPTP
LOCUS
            RATPTP
                                     1746 bp
                                                TERNA.
                                                         linear
                                                                  ROD 27-APR-1993
DEFINITION
            Rattus norvegicus potassium channel protein mRNA, complete cds.
ACCESSION
            M26161
VERSION
            M26161.1 GI:206490
KEYWORDS
            potassium channel protein.
SOURCE
            Rattus norvegicus (Norway rat)
  ORGANISM
            Rattue norvegious
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Eutaleostomi;
            Manmalia; Butheria; Rodentia; Sciurognathi; Muridae; Murinae;
            Rattus.
REFERENCE
                (bases 1 to 1746)
  AUTRORE
            Christie, M.J., Adelman, J.P., Douglass, J. and North, R.A.
  TITLE
            Expression of a cloned rat brain potassium channel in Kenopus
            cocytes
  JOURNAL
            Science 244 (4901), 221-224 (1989)
  MEDLINE
            89203264
   PURMED
            2539643
COMMENT
            Original source text: Rattus norvegicus cDNA to mRNA.
FEATURES
                      Location/Qualifiers
                      1. .1746
     BOUTCO
                      /organism="Rattus norvegicus"
                      /mol_type="mRNA"
                      /db_kref="taxxx:10116"
                      1. .1746
     gene
                      /gene="potsssium channal"
     CDS
                      35. .1522
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                      /product="potassium channel protein"
                      /protein_id="AAA41982.1"
                      /db xref="GI:206491"
                      /translation="MTVMSGENADEASAAPGHPQDGSYPRQADHDDHECCERVVINIS
                      GLRFETQLKTLAQFDNTLLCMPKKRMRYFDPLRNEYFFDRNRPSFDAILYYYQSGCPL
                      RRPVNVPLDMPSEEIKPYELGEEAMRKFREDEGFIKEEERDLPEKEYOROVWLLFEYD
                      ESSGPARVIAIVSVMVILISIVIPCLETLPELEDDXOFTGTIHRIDHTTVIYTSNIFT
                      DPFFIVETLC:IWP8FELVVRFFACPSKTDFFKNIMNFIDIVAIIPYFITLGTEIARQ
                      egnoxgeoatsla1lrvirlvrvfrifkl9rkskglq1lgqtlkaskrelqll1fflf
                      igvilpsbavyparaeeaeshfssipdavwmavvemttvgygdmypvtiggkivgslc
                      atagvi/tialpvpvivsnfnyfyhretegegaglihvsspnlasdsdlsrrssstis
                      KSBYMBIBEDMINSIAHYRQANIRTGNCTATDQNCVNK8K1LTDV"
ORIGIN
                          93.3%; Score 44.8; DB 10; Length 1746; 95.8%; Pred, No. 1.3e-07;
  Query Match
  Best Local Similarity
  Matchas
                                 0; Mismatches
           46; Conservative
                                                        Indele
                                                                   0; Gaps
                                                                                0;
Qy
            1 GATCCTGGGCCAGACCCTCAAAGCTAGTATGAGAGAGCTAGGGCTGCT 40
          973 GATOCTOGGCCAGACCCTCAAAGCTAGTATGAGGGAGTTAGGGCTGCT 1020
DЪ
```

Sequence Comparison B

```
RESCILT 4
HUMVENHK1
LOCUS
             HUMVENHKI.
                                     2445 bp
                                                 TURNA
                                                         linear
                                                                  PRI 14-JAN-1995
            Human voltage-gated potassium channel (HK1) mRNA, complete cds.
DEFINITION
ACCESSION
             M60450
VERSION
             M60450.1 GI:308762
KEYWORDS
             voltage-gated potassium channel.
SOURCE
             Homo sapiene (human)
  organism
             Homo sapiens
             Bukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleoetomi;
             Mammalia; Euthoria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE
                (bases 1 to 2445)
             Tamkun, N.M., Knoth, K.M., Walbridge, J.A., Kroemer, H., Roden, D.M. and
  AUTHORS
            Glover, D.M.
  TITLE
             Molecular cloning and characterization of two voltage-gated K+
             channel cDNAs from human ventricle
             FASEB J. 5 (3), 331-337 (1991)
  JOURNAL
  MEDLINE
             91160866
   PUBNED
             2001794
COMMENT
            Original source text: Homo sepiens ventricular cardiac muscle cDNA
             to mRNA.
PEATURES
                      Location/Qualifiers
     source
                      1. .2445
                      /organism="Homo sapiens"
                      /mol_type="mRNA"
                      /db xref="taxon:9606"
                      /tipouo_typo-"ventricular cardiac musclo"
     Gene
                      1. .2445
                      /gene="HK1"
     ന്നട
                      290. .2259
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                      /standard_name="KCNA4"
                      /codon_start=1
                      /product="voltage-gated potassium channel*
                      /protein_id="AAA61275.1"
                      /db_xref="GI:308763*
                      /db_xref="GDB:G00-120-044"
                      /translation="MEVAMVHAESSGCMSHMPYGYAAQARARERERLAMSRAAAAAV
                      aaataavegegggggehehiqergactehdpqeergerrrrqreekkkahyrqeep
                      PHCSDLMPSGSEEKI LRELSEEEEBEEEEEEEEEEGRFYYSEDDHGDECSYTDLL PQD
                      egggyssvry6dccervvinv8glrfbtonktlaqffbtillgdpbkrtqyfd9lrnb
                      YP BDRNR PS FDAILYYY QSGRLKR PVN V PFDI FTE EVK FY QLJE EALLK FREDEG FV
                     reeedralpenefkkqiwllfeypbssspargiaivsvlvilisivifcletldrfrd
                     DRDLVMALSAGGHGGLLNDTBAPHLENSGHTIFNDPPFIVETVCIVWFSFEFVVRCFA
                      CPSQALPPKNIMNIIDIVSILPYFITLGTDLAQQQGGGNGQQQQAMSFAILRIIRLVR
                     VPRIPKLSRHSKGLQILGHTLRASMRRIGLLIFFLPIGVILFSSAVYFARADEPTTHF
                     Q9IPDAFWWWVTMTTVGYGDMKPITVGGKIVG9LCAIAGVLTIALPVPVIVENFNYF
                     YHRBTENEEQTQLTQMAVSCPYLPSNLLKKFRSSTSSSLGDKSEYLEMREGVKESLCA
                     KEEKCQGKGDD6ETDKWNCSNARAVETDV"
ORIGIN
                          100.0%; Score 48; DB 9; Length 2445; 100.0%; Pred. No. 1.1e-05;
  Query Match
  Best Local Similarity
  Matches
                                  0; Mismatches
           48; Conservative
                                                     0:
                                                        Indala
                                                                    0;
                                                                        Gaps
Qy
            1 QATCCTGGGCCACACCCTCAGAGCCAGCATGCGGGAACTGGGCCTTCT 48
         1692 GATCCTGGGCCACCCTCAGAGCCAGCATGCGGGAACTGGGCCTTCT 1739
Db
```

Sequence Comparison C

```
RESULT 4
HUMVENHK1
                                    2445 bp
            HUMVRNHK)
                                               mRNA
                                                               PRI 14-JAN-1995
LOCUS
                                                       linear
DEFINITION
            Human voltage-gated potassium channel (HK1) mRNA, complete cds.
ACCESSION
            M60450
VERSION
            M60450.1 GI:308762
KEYWORDS
            voltage-gated potessium channel.
            Homo sapiens (human)
SOURCE
  ORGANISM
            Home sapians
            Eukaryota: Metasoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia, Eutheria; Primates; Catarrhini; Rominidae; Homo.
REFERENCE
               (bases 1 to 2445)
  AUTHORS
            Tamkun, M.M., Knoth, K.M., Walbridge, J.A., Krosmer, H., Roden, D.M. and
            Glover, D.M.
  TITLE
            Molecular cloning and characterization of two voltage-gated K+
            channel cDNAs from human vehtricle
  JOURNAL
            FASEB J. 5 (3), 391-337 (1991)
  MEDLINE
            91160866
            2001794
   PUBMIKO
COMMENT
            Original source text: Homo sapiens ventricular cardiac muscle cDNA
            to MRNA.
PRATURES
                     Location/Qualifiers
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                     /organiem-"Homo sapiene"
                     /mol_type="mRMA"
                     /db_xref="taxon:9606"
                     /tissue_type="ventricular cardiac muscle"
                     1. .2445
     gene
                     /gene="HKl"
                     298. .2259
     ෆ8
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                     /etandard_name="Kv1.4"
                     /standard_name="KCNA4"
                     /codon_start=1
                     /product "voltage-gated potassium channel"
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Sequence Comparison D

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VERSION
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REPERENCE
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             Leicher, T., Roeper, J., Weber, K., Wang, K. and Pongs, O.
  TITLE
             Structural and functional characterization of human potassium
             channel subunit beta 1 (KCNA1B)
  JOURNAL
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                (bases 1 to 1624)
  AUTHORS
             Leicher. T.
             Direct Submission
  TITLE
  JOURNAL
             Submitted (02-DBC-1994) T. Leicher, Zentrum fuer Molekulare
             Neurobiologie, Abt. Prof. Pongs, UKE Hamburg-ZMNH II Haus 42,
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